

REMARKS

After the foregoing Amendment, claims 93 – 95, 114 – 171, 174 and 185 - 189 are currently pending in this application. Claims 93, 95, 114 – 171 and 174 were previously withdrawn from consideration. Claims 96 – 113, 172 – 173, and 175 – 184 are cancelled without prejudice. Claim 94 is amended without prejudice and claims 185 – 189 are added. Support for the amendment and new claims can be found in original claim 94, original claim 96, and paragraphs [0034] – [0050] of the specification. Applicant submits that no new matter is introduced into the application.

Objections to the Specification

The Action objects to the specification because of specific informalities. In particular, the Action objects to obvious spelling and translation errors with obvious corrections. Amendments to the specification obviate the objection and withdrawal of the same is respectfully requested.

Claim Rejections - 35 USC §112, first paragraph - enablement

The Action rejects claims 97 – 104 and 106 – 108 as lacking enabling support in the specification. Applicant respectfully submits that all of these claims are enabled. Nonetheless, each of these claims is cancelled without prejudice only in an earnest effort to advance prosecution. The rejection is moot.

Claim Rejections - 35 USC §112, second paragraph

The Action rejects claims 96 – 109, 111 – 113, 172 – 173, and 175 – 184 as indefinite. Applicant respectfully submits that all of these claims are definite. Nonetheless, each of these claims is cancelled without prejudice only in an earnest effort to advance prosecution. The rejection is moot.

Claim Rejections - 35 USC §101

The Action rejects claims 97 – 108, 111 – 112, 172 – 173, and 175 - 184 as process claims lacking any steps. Applicant respectfully submits that every one of these claims is directed to a composition where the further limitations define the structure of the claimed compound. Nonetheless, each of these claims is cancelled without prejudice only in an earnest effort to advance prosecution. The rejection is moot.

Claim Rejections - 35 USC §102

The Action rejects claims under 35 U.S.C. §102 over several different references. As set forth below, none of the references disclose all of the elements of claim 94, as amended. Claim 1, as amended, recites:

...Y is a nitrogen atom (N) within a moiety selected from the group consisting of N,N-dimethyl-1-phenethylamine (dmpa), pyridinyl-phenyl-ethyne, 1-phenyl-3-N,N-dimethylamine-propyne....

Ananias

The Action rejects claims 94, 97 – 113, 172 – 173, and 175 – 184 under 35 U.S.C. §102(b) as anticipated by Ananias, (2001) Transition Metal Chemistry 26 (4 – 5): 570 – 573 (“Ananias”). Claims 97 – 113, 172 – 173, and 175 – 184 are cancelled and the rejection of each is moot.

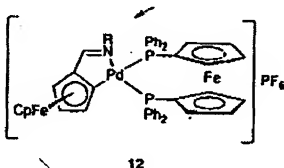
The Action states that Ananias “anticipates the claims when $X = \text{NCO}$, $\text{L-L} = \text{Fe}(\text{C}_5\text{H}_4\text{PPh}_2)_2$ and the R-substituents are H and $\text{C} - \text{Y} = \text{N}$, N, dimethylbenzylamine.” According to this characterization, Ananias only discloses that “ $\text{C} - \text{Y} = \text{N}$, N, dimethylbenzylamine.” As the Action admits, Ananias does not disclose Y as recited in claim 94 and quoted above. Ananias does not disclose every element of claim 94.

Based on the foregoing, Ananias cannot anticipate the claims. Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §102(b) over Ananias.

Vila

The Action rejects claims 94, 97 – 113, 172 – 173, and 175 – 184 under 35 U.S.C. §102(b) as anticipated by Vila *et al.* (2001) J. Organometallic Chem. 637 – 639: 577 – 585 (“Vila”). Claims 97 – 113, 172 – 173, and 175 – 184 are cancelled and the rejection of each is moot.

The Action states that Vila anticipates the claims when "X = PF₆, L-L = Fe(C₅H₄PPh₂)₂ and the R-substituents are H and C-Y = substituted aryl group." The particular aryl disclosed in Vila and illustrated in the Action is copied below:



Vila discloses synthesis via schiff base metallation agents, which lead to the N = C double bond shown above. As the Action admits and as shown above, Vila does not disclose "Y" as recited in claim 94.

Based on the foregoing, Vila does not disclose every element of claim 94 and cannot anticipate the claim. Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §102(b) over Vila.

Lousame

The Action rejects claims 94, 97 – 113, 172 – 173, and 175 – 184 under 35 U.S.C. §102(b) as anticipated by Lousame *et al.*, (2000) J. Inorg. Chem.: 2055 – 2062 ("Lousame"). Claims 97 – 113, 172 – 173, and 175 – 184 are cancelled and the rejection of each is moot.

The Action states that Lousame anticipates the claims when “X = ClO₄, L-L – Ph₂PC₅H₄FeC₅H₄PPh₂-P,P’ and the R-substituents are H and C-Y = substituted aryl group, which is , C₆H₄C=NC(Me)=C(Me)NMe.”

Lousame discloses synthesis via phenylimidazole as a cyclometallation reagent, which leads to structures including the C = N double bond described in the Action. As the Action admits, Lousame does not disclose “Y” as recited in claim 94.

Based on the foregoing, Lousame does not disclose every element of claim 94 and cannot anticipate the claim. Applicant respectfully requests withdrawal of the 35 U.S.C. §102(b) rejection over Lousame.

Ma

The Action rejects claims 94, 97 – 113, 172 – 173, and 175 – 184 under 35 U.S.C. §102(b) as anticipated by Ma, Jian-Fang, *et al.*, (2000) *Inorganica Chimica Acta.*: 164 – 171 (“Ma”). Claims 97 – 113, 172 – 173, and 175 – 184 are cancelled and the rejection of each is moot.

The Action states Ma anticipates the claims based on its “structure 3” when “X = PF₆, L-L – Fe(C₅H₄PPh₂)₂ and the R-substituents are H and C-Y = substituted aryl group.”

As stated in its title, Ma discloses N,N-dimethylbenzylamines as the starting reagent, which results in the lack of a chiral center. Further, the Action admits that Ma does not disclose “Y” as recited in claim 94.

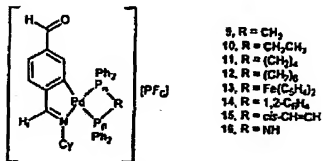
Based on the foregoing, Ma does not disclose every element of claim 94 and cannot anticipate the claim. Applicant respectfully requests withdrawal of the 35 U.S.C. §102(b) rejection over Ma.

Ares

The Action rejects claims 94, 97 – 113, 172 – 173, and 175 – 184 under 35 U.S.C. §102(a) over Ares et al., (2002) Polyhedron: 2309 – 2315 (“Ares”). Claims 97 – 113, 172 – 173, and 175 – 184 are cancelled and the rejection of each is moot.

Ares was available online at the earliest by September 11, 2002 and officially published October 1, 2002. In contrast, under 35 U.S.C. §365, this application is entitled to priority to August 30, 2002. Ares is not prior art.

Assuming *arguendo* that Ares was prior art, the Action states that Ares anticipates the claims based on its Scheme 1 when “X = PF₆, L-L = Fe(C₅H₄PPh₂)₂ and the R-substituents are H and C-Y = substituted aryl group.” Ares Scheme 1, as shown in the Action, and its corresponding aryl group, is reproduced below:



Scheme 1.

The Action admits, as shown above, that Ares does not disclose “Y” as recited in claim 94.

Based on the foregoing, Ares is not prior art, Ares cannot be used to reject the claims, and the rejection is improper. Even if Ares were prior art, Ares does not disclose every element of claim 94 and could not anticipate the claim. Applicant respectfully requests withdrawal of the 35 U.S.C. §102(b) rejection over Ares.

New claims 185 – 189 depend on claim 94 and include its elements. For the same reasons set forth above, none of the cited prior art anticipates new claims 185 – 189.

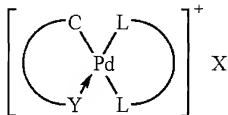
Claim Rejections - 35 USC §103

The Action rejects claim 96 as obvious over Ananias. Claim 96 is cancelled and its rejection is moot. Claim 94 is amended to include the limitations of claim 96.

The Action states that Ananias teaches $[\text{Pd}(\text{N},\text{C-dmba})(\text{dppf})][\text{NCO}]\cdot\text{CH}_2\text{Cl}_2$, and admits that this structure differs from the claimed compounds. According to the Action, the elected species, dmpa, differs in the substitution of a hydrogen in Ananias’s structure for a methyl group in the claimed structure. But the Action states that a study of Ananias “clearly demonstrates that the instant elected species is a homolog of dmba.” The Action also states that it “would have been obvious to ...

select a homolog akin to the group of Ananais [*sic*] et al. with the expectation that the species would have the utility of the other homolog.”

As the Action admits, Ananias does not disclose a cyclopalladated compound corresponding to the structure

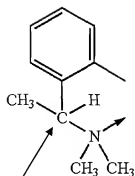


where, as recited in amended claim 94:

Y is a nitrogen atom (N) within a moiety selected from the group consisting of N,N-dimethyl-1-phenethylamine (dmpa), pyridinyl-phenyl-ethene, 1-phenyl-3-N,N-dimethylamine-propene;

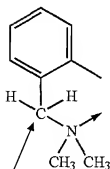
C is selected from the group consisting of a carbon atom at the ortho position of the dmpa, a carbon atom within the pyridinyl-phenyl-ethene, a carbon atom within the 1-phenyl-3-N,N-dimethylamine-propene; and the carbon atom is covalently bonded to the atom of palladium; the ring containing C, Y and Pd can be constituted of three to eight atoms;

Underlining emphasis added. The specification's scheme 5 and scheme 3, reproduced below, illustrate compounds derived from dmpa versus dmbs. See the specification at pages 10 – 12, paragraphs [0034] – [0050].



dmpa
Scheme 5

Chiral Center



dmbs
Scheme 3

Non-Chiral Carbon

A homolog is a compound that differs regularly from a starting compound by “successive addition of the same chemical group, e.g., by $-\text{CH}_2$.” MPEP §2144.09 II. Although, a methyl is added according to Scheme 5, the addition is not the successive addition of a spacer such as $-\text{CH}_2$. Instead, the addition results in the fundamental different property of chirality. See the specification at page 10 – 12, paragraphs [0034] – [0050]. Given this dramatic property shift, one of ordinary skill in the art would not know that the structural change could be made. And even if made, extensive testing would be required to determine if the new structure included a biological property. In other words, there is a structural discontinuity between the compound derived from dmpa versus Ananias's dmbs derived compound. Dmpa and dmbs are not homologs.

As stated in the specification, dmmpa derived cyclopalladated compounds have properties that differ from non-chiral counterparts:

From the presented results, it became clear that, for the R(+) enantiomer, inhibiting doses IC_{50} are about 10 times higher in comparison to those observed for the S(-) enantiomer. This fact shows an enantioselective dependence from the cytotoxicity process caused by the compounds, showing higher efficiency of the compounds having the S(-) isomer from dmmpa in their structure.

Paragraph [00169]. Further examples provided in the specification provide evidence that the choice of enantiomer used in an assay or treatment is determinative of the outcome. In other words, the ability to select the enantiomer used in a particular application is important to achieve improved results. Ananias's dmmpa derived cyclopalladated compounds cannot possess this activity and thus they do not include sufficient properties to be considered similar to the claimed compounds under MPEP §2144.09. Further, Ananias includes no teaching of the importance of selecting enantiomers or any suggesting that such a selection would lead to improved results. One of ordinary skill in the art would not expect improved results due to the substitution of Ananias's hydrogen with a methyl group, as in the claimed compounds.

Ananias mentions that generic "[cyclopalladated complexes ... have been used as pathways to new products in [unnamed] antitumor [applications]]. Ananias at page 570, left column. But Ananias is in fact devoid of any teaching that any one of the specific compounds disclosed has any biological property. Ananias does not

teach any biological effect of its compounds. On that basis, Ananias cannot teach that creating a chiral center, as in the claimed compounds, would have any biological effect.

Ananias describes a steric feature of the disclosed compounds but teaches that the hinderance is related to ligand (*i.e.*, dpf) binding:

The opening of the cyclometallated ring, for (1a) and (2a), in the solid state suggests influence of a steric nature; in this way there would be a better accommodation for the ligands within the palladium coordination sphere.

Ananias at 573, left column. Based on this passage, one of ordinary skill in the art would conclude that introduction of further steric hinderance may decrease cyclopalladated compound formation. Ananias teaches away from substituting the hydrogen with a methyl group; *i.e.*, away from the claimed compounds. One of ordinary skill in the art would not be motivated to substitute the hydrogen in Ananias's compound with a methyl group.

Based on the foregoing, the claims, as amended, are not obvious and the Applicant believes that the rejection under 35 U.S.C. §103 is overcome. Applicant respectfully requests withdrawal of the 35 U.S.C. §103 rejection.

New claims 185 – 189 include the elements of claim 94 by dependence. For the same reasons set forth above, new claims 185 – 189 cannot be obvious over Ananias.

Applicant: Cairés et al.
Application No.: 10/525,781

Conclusion

If the Examiner believes that any additional matters need to be addressed in order to place this application in condition for allowance, or that a telephone interview will help to materially advance the prosecution of this application, the Examiner is invited to contact the undersigned by telephone at the Examiner's convenience.

In view of the foregoing amendment and remarks, Applicant respectfully submits that the present application, including claims 94 and 185 - 189, is in condition for allowance and a notice to that effect is respectfully requested.

Respectfully submitted,

Cairés et al.

By/Douglas J. Bucklin/
Douglas J. Bucklin
Registration No. 51,208

Volpe and Koenig, P.C.
United Plaza, Suite 1600
30 South 17th Street
Philadelphia, PA 19103
Telephone: (215) 568-6400
Facsimile: (215) 568-6499

DJB/vag